

TRF1 As A Major Contributor For Telomeres' Shortening In The Context Of Obesity

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Abstract

Obesity is a prevalent multifactorial chronic disorder characterized by metabolic dysregulation. Sustained pro-oxidative mediators trigger harmful consequences that reflect at systemic level and contribute for the establishment of a premature senescent phenotype associated with macromolecular damage (DNA, protein, and lipids). Telomeres are structures that protect chromosome ends and are associated with a six-protein complex called the shelterin complex and subject to regulation. Under pro-oxidant conditions, telomere attrition and the altered expression of the shelterin proteins are central for the establishment of many pathophysiological conditions such as obesity. Thus, considering that individuals with obesity display a systemic oxidative stress profile that may compromise the telomeres length or its regulation, the aim of this study was to investigate telomere homeostasis in patients with obesity and explore broad/systemic associations with the expression of shelterin genes and the plasma redox state. We performed a cross-sectional study in 39 patients with obesity and 27 eutrophic subjects. Telomere length (T/S ratio) and gene expression of shelterin components were performed in peripheral blood mononuclear cells by qPCR. The oxidative damage (lipid peroxidation and protein carbonylation) and non-enzymatic antioxidant system (total radical-trapping antioxidant potential/reactivity, sulfhydryl and GSH content) were evaluated in plasma. Our results demonstrate that independently of comorbidities, individuals with obesity had significantly shorter telomeres, augmented expression of negative regulators of the shelterin complex, increased lipid peroxidation and higher oxidized protein levels associated with increased non-enzymatic antioxidant defenses. Principal component analysis revealed TRF1 as a major contributor for firstly telomeres shortening. In conclusion, our study is first showing a comprehensive analysis of telomeres in the context of obesity, associated with dysregulation of the shelterin components that was partially explained by TRF1

upregulation that could not be reversed by the observed adaptive non-enzymatic antioxidant response.

Keywords

Aging; Obesity; Oxidative Stress; Shelterin Complex; Telomere Length; TRF1.